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HEREDITARY CEREBELLAR ATAXIA, WITH REPORT OF A CASE.*

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In 1893 Marie[1] grouped together two cases reported by Fraser[2], three by Nonne[3], eight by Sanger Brown[4], and three by Klippel and Durante[5], and gave to them the name *hérédo-ataxie cérébelleuse.* It was a bold thing to do! Deliberately to make an addition to the nosology of nervous diseases without having had an opportunity to personally study a single example of the new malady, savored somewhat of genius—or of effrontery. Just which of these two elements dominated the situation remains to be seen, for after more than eight years of deliberation by many neurologists and the report of a number of cases in various countries, the assumption of Marie remains neither substantiated nor fully refuted. It is still *sub judice.*

The obstacles in the way of establishing hereditary cerebellar ataxia as a distinct disease are several: first, a fundamental barrier, diversity of symptoms in the original basic sixteen cases; second, absence of uniformity of subsequent cases reported as examples of this disease; third, lack of careful post-mortem examinations in cases which were, clinically, sufficiently typical; and, fourth, variation in post-mortem findings. To these may now be added, fifth, several autopsies which strongly tend to controvert Marie's thesis.

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To establish the new type it is first necessary to segregate the cases from those of accidental family type due to lues[6], parturition injury and the like, from hereditary quadriplegia with incoördination[7], from Friedreich's disease and from certain cases of indeterminate nature, not yet classified, affecting cerebrum and cerebellum or cerebrum, cerebellum and cord; and then the cases so separated must be shown to be sufficiently similar in clinical manifestations and structural changes to allow of amalgamation into a pathological solidarity. In the attempt to fulfil the first of these conditions the greatest difficulty arises in drawing the line between the proposed group and Friedreich's ataxia, and in selecting cases from the heterogeneous mass of more complicated diseases characterized clinically by progressive incoördination with preserved or exaggerated reflexes. Owing principally to lack of material and as yet inadequate knowledge, but to some extent also to loose methods, neither condition can be said to have been met.

A succinct statement of Marie's claim with brief mention of the basal and some of the later reported cases will elucidate the present status of the question. Although none of the basal cases had been reported as Friedreich's ataxia, Marie devotes a large part of his paper to a differentiation of his new type from this disease. The prominent features of Friedreich's ataxia, it will be remembered, are family type, inception before fourteenth or sixteenth year, incoördination in station and progression, rather of the staggering than the spinal ataxic sort and often not increased by closure of the eyes; movement of the upper extremities characterized by disorder resembling intention tremor, but at the same time oscillatory and choreiform; speech slow, uncertain or explosive; loss of deep reflexes; integrity of pupillary reactions, ocular muscles and optic nerve; presence of nystagmus, deformity of the feet and spinal curvature; unimportance of sensory and mental symptoms.

In contrast, Marie predicates of his group, hereditary as well as family type, inception after twenty, exaggeration or at least presence of the deep reflexes, defective pupillary reactions, involvement of the optic nerve and ocular muscles, and absence of deformity. In mode of onset and progress, character of motor disorder, frequent absence of Romberg's sign, presence of nystagmoid jerking, defect of speech, unimportance of mental symptoms and lack of prominence of sensory troubles, the two affections are so nearly identical as not to admit of definite distinction. Marie further laid great stress on the totally different pathological anatomy of the two diseases, affirming for his type atrophy of the cerebellum as the structural basis, instead of the combined sclerosis known to be present in the ataxia of Friedreich. Indeed, the qualification "cérébelleuse" was added to the title purely on this assumption.

Let us see what the basal cases show. Fraser reported his as "Defect of Cerebellum Occurring in a Brother and Sister." The disease began in infancy or early childhood, and was characterized by incoördination, ocular paralysis, slow hesitating speech and, in one case, by slow pupils and vertigo on assuming the supine position. Nothing is said as to reflexes.

Nonne made no attempt to classify his cases (three brothers), calling the affection simply "A singular disease of the central nervous system." Symptoms began at ten, fourteen and in middle life respectively, and the patients exhibited incoördination, preserved deep reflexes, eye symptoms, incoördinate speech and some mental weakness.

Brown reported his cases as "Hereditary ataxia," recognizing that they constituted a group quite distinct from previously classified forms, remarked that if they were to be accepted as instances of Friedreich's ataxia, the criteria of this disease should be considerably modified, but ventured no opinion as to classification. In this truly remarkable series of more than twenty cases, the disease was traced through four generations and was found to preserve a tolerably determinate form. In addition to ataxia, the principal characteristics were:—onset after early childhood (11th to 45th year), optic atrophy, ptosis, impaired pupillary reflexes, exaggeration of knee-jerks, and imperfect articulation; no sensory symptoms, disturbance of the muscular sense, spinal curvature or club foot. In commenting upon these cases both Omerod[8] and Bernhardt[9] compared them with those of Nonne and also with the case, or rather cases, of Menzel, presently to be mentioned, and both were unwilling to allow that Brown's cases constituted an aberrant form of Friedreich's disease, but neither ventured to assert identity of the type with those of Nonne.

Klippel and Durante were also non-committal as to the nature of their cases, entitling their communication "Contribution to the study of family and hereditary nervous affections." Their patients, two brothers and a sister, like most of the others presented incoördination, impaired speech and eye troubles, but unlike the others, also sensory symptoms, scoliosis and club-foot (pes cavus).

Passing now to the pathological basis of the new disease we find a foundation insufficient in both extent and uniformity. At the time of Marie's paper he could refer to only two autopsies; one each by Fraser and Nonne. In Fraser's case the cerebellum was found to be small (one-half the normal weight), the Purkinje cells diminished in number and altered in form. There were also cystic collections of fluid between the convolutions, which the author considered to be unimportant. Apparently the cord was not examined. In the case of Nonne the cerebellum (with pons and medulla) weighed only 70 per cent. of the normal, but the cerebrum was also small (87 per cent. of normal) and the cord proportionately smaller than either. Squaring the average diameter of the cord and multiplying this by the length, as a basis of comparison of bulk, I find that the cord of the patient was in total size only 44 per cent. of normal. Clearly, to assert atrophy of the cerebellum as the essential and basic lesion in this case is to approach seriously near to the absurd—the more so as an exhaustive microscopic examination failed to reveal anything abnormal except in the proportion of coarse and fine fibers in the nerve roots of the cord and in some of the peripheral nerves.

Marie has, indeed, as Nonne[10] says, drawn the boundaries rather wide. To make this fact graphically apparent, I have constructed the accompanying table, from which it is readily seen that while each of the four sets of cases remains reasonably constant to its own type, all the cases agree in only two particulars—incoördination and family type—although nearly all showed present or exaggerated reflexes. In addition it may be specially noted that excepting only the cases of Sanger Brown, there is no conclusive evidence of direct heredity.

The basal cases, then, are constant to each other in neither heredity, age at onset, rate of progress, eye symptoms, sensory symptoms, speech, mental disorder, condition of reflexes, nor post-mortem findings. Subsequent contributions have not as yet served to crystallize a type or even to simplify the complexities of the subject, as, I think, a brief review will show.

Since Marie's publication three of Sanger Brown's cases have come to autopsy and in one of these (No. VI.) a microscopic examination has been made by Dr. Adolf Meyer[11]. As no notes were made at the time of the autopsy[12], the exact size of the different parts of the nervous system is not known, but there was no striking diminution in the size of any part, and Meyer says, "There is no circumscribed cerebellar lesion, nor does the cortex show a marked decrease of the number of Purkinje cells." The cervical cord showed changes very similar to those found in Friedreich's disease. In other words, this autopsy lends no support to Marie's claim. As Meyer very moderately puts it, "The separation of a *type cérébellaire* is clinically justified, but anatomically to less extent than Marie seemed to expect. The material of the other two au-

Cases and Reporter	Heredity	Number of cases in same family	Age at onset	Deep reflexes	Optic atrophy	Ptosis	Ocular paralysis	Nystagmus	Pupils	Speech	Mental	Autopsy	Remarks
Fraser 1	None	2	2-3		None [2]	None	Present	None		Slow, hesitating	Normal	Small cerebellum. Cell changes	Uneasy movements of eyes
2	None	2	About 2-3		”	”	”		Slow	Slow	”		
Nonne 1	None	3	25-30	Present	Present	None	Paresis	Present	Sluggish to accom.	Irregular	Slight acute dementia	Small nervous system	
2	None	3	14	Slightly exagger.	”	”	”	”	L X R	Explosive	Slow		
3	None	3	10	Brisk	”	”	”	”	Normal	Incoordinate	Weak		
Brown 1	Present	4	18	Exaggerated	Present	Present	None	None	Slow	Slow	Normal	Cerebellum normal. Cord changes	The autopsy of Meyer was made on case not personally examined by Brown—not one of the eight
2	”	4	20	”	Probably beginning	”	”	”	”	Slightly difficult	”		
3	”	4	18	”	Present	”		”	”	Defective	”	Cerebellum normal. Cord changes	
Incipient 4	”	4	21	”				”		Slow			
5	”	1	35	Absent*	Present	Present	Present	”	No reac. to light	Defective	Memory slightly impaired		
6	”	2	31	Exaggerated	”	”	None	”	Slow	”	Normal		
7	”	4	35	”	”	None	”	”	Slight reaction to light	”	”		
8	”	3	40	”	”	”	”	”		Slightly defective	”		
Klippel & Durante 1	”	3	26-27	Present	Absent	None	None	Present	To light—To accom. slight	Indistinct hesitating	Memory slightly weak		
2	”	3	33	Feeble or absent[1]	”	”	”	None	Varied[3]	Ataxic		Changes in cord & cerebell'm	
3	”	3	35	Present	Present	”	Present	Present	Normal	Slow, defective		do	

*Not to be elicited on account of contractures. [1]In 1888 knee-jerks were diminished, in 1894 gone. [2]Londe is mistaken in reporting optic atrophy present in these cases. [3]In 1888, reaction normal; in 1892, lost; in 1894, slight.

topsies (cases 18 and 20 of Dr. Brown's diagram) is now in process of examination by Dr. Lewellys F. Barker*

One of the first to accord recognition to Marie's disease was Brissaud[13] but he did so with some reserve, insisting that although *hérédo-ataxie cérébelleuse* might be essentially different from Friedreich's disease, its systemic localization was nearly the same, and acknowledging that if his patient had only had absence instead of exaggeration of the deep reflexes he would instantly have made a diagnosis of Friedreich's ataxia. Later in the same year Londe[14] published a report of two additional cases which likewise were to be distinguished from Friedreich's disease only by the exaggeration of the reflexes.

Quite the most complete treatment of the subject is the later monograph of this author[15], who bases his description on the cases already mentioned, two of Erb[16], and two of Seeligmüller[17].

The patients of Erb were two sisters, aged twenty-two and eleven years, in whom the disease had existed for sixteen and four years respectively. The knee-jerks were "very lively" or "exaggerated." Erb demonstrated the cases as examples of Friedreich's disease, and indeed, aside from the condition of the knee-jerks, there seems to be no possible reason for calling them anything else.

I have found only an abstract of Seeligmüller's cases, but they appear to belong neither to Friedreich's nor Marie's disease. Indeed, Londe frankly says that he is unable to classify them, but as they showed incoördination and lively knee-jerks, he puts them in as cases of *hérédo-ataxie cérébelleuse*—a rather feeble excuse, it seems to me.

In a paper published several years after the one that Marie made use of, Nonne[18] reported six more peculiar cases marked especially by incoördination, and therein he distinctly declines to support the dictum of Marie, not only calling attention to the fact that the basal cases of this author differed in some of the fundamental symptoms, but also insisting that transition forms could be found bridging all the differences between Friedreich's ataxia, cerebellar atrophy, Marie's type and other entirely unclassified forms of disease. Indeed, four of the cases reported in this second paper are particularly good examples of these connecting links.

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*See statement of Dr. Barker, second paragraph before report of my case.

Another stumbling block is the case of Menzel[19]. Why it should be excluded, as it is by Marie, or considered as intermediate, as it is by Londe, is not clear, in the presence of family character, onset relatively late (twenty-eight years), incoördination of all extremities, pupillary signs and exaggeration of the knee-jerks. But Marie probably considered that he could not include it in his type because the anatomical changes did not agree with what he thought *they ought to be*. Besides atrophy (or rather aplasia) of cerebellum and pons, there was the cord degeneration typical of Friedreich's disease. In the absence of autopsy I am inclined to think he would have made the case of Menzel part of his foundation. As it is, he mentions the post-mortem as showing the lesions of both hereditary cerebellar ataxia and Friedreich's disease, and intimates that therein is cause to give us pause.

In 1893 Senator[20] published what he believed to be an incipient case of Friedreich's ataxia and expressed the opinion that the disease is essentially a congenital atrophy of the cerebellum, or important parts thereof, accompanied by congenital atrophy of the spinal cord. This position was very warmly attacked by Schultze[21] who asserted that the case was not one of Friedreich's disease at all because the knee-jerks were present and there was no locomotor (only static) ataxia. In a second paper, Senator[22] valiantly defended his opinion, and, clinically, at least, had rather the better of the argument as by that time the knee-jerk had quite disappeared on one side and almost on the other.

Two years before the paper of Marie, Fornario[23] recorded three cases of hereditary ataxia (two brothers and a sister) anomalous in several respects. The second one exhibited exaggerated knee-jerks, but later the jerk diminished on one side. Discussing his cases the author in a measure anticipates Marie but is much more conservative. He called attention to the difficulty of clinical distinction between the cerebellar, spinal and combination cases, and seemed to assume a chiefly cerebellar origin for Friedreich's disease.

The case of Menzel, just noted, early showed exaggerated knee-jerks while later they were hardly to be elicited, and one of the patients of Klippel and Durante, as noted in my table, exhibited at the time of examination normal knee-jerks while two years later Oulmont and Ramond[24] found them absent.

In a recent number of *Brain,* Howard Gladstone[25] describes a case of Friedreich's ataxia with presence of the knee-jerks and ankle-clonus. Not only was the case sufficiently typical, with the exception of the reflexes, but it was comparatively advanced, and a younger brother had the same disease much less advanced but with loss of deep reflexes. Starr[26] reports a case adhering to the type of Friedreich in all essentials, except that "the knee-jerks were very much exaggerated," and avows the as yet inadequacy of distinction between this disease and that of Marie.

Of two sisters with Friedreich's disease described by Raymond[27] one had brisk knee-jerks and the other none. I have myself seen a sufficiently typical and well-advanced case of Friedreich's disease in which the knee-jerks were present although they had been diminishing for some time, and Hodge[28] mentions three cases, all with marked increase of the knee-jerk. The disease began at twelve, fourteen and fifteen respectively, and the patients were still living at forty-four, forty, and thirty-nine years.

From the clinic of Erb, Paravicini[29] reports a case of what he calls cerebello-spinal ataxia inasmuch as it partook of the clinical features of both Friedreich's disease and *hérédo-ataxic cérébelleuse.* To the ordinary symptoms of the former were added rigid pupils and ocular paralyses, but optic atrophy was wanting.

The two cases reported as hereditary cerebellar ataxia by K. Miura[30], correspond clinically very closely to the type of Marie, but a most careful post-mortem examination of the first one revealed simply diminution in size of pons, medulla, cord and cerebellum, without microscopic change.

A series approximating that of Sanger Brown in extent and interest is recorded by Lennmalm[31]. Of thirty-three members of the family in several generations, eight seem to have had the disease and of these the author reports three—a young woman of twenty-two, her mother *aet.* fifty-two, and a maternal aunt *aet.* forty-five. They were characterized by late inception (13, 43 and 26 years respectively), gradually appearing and progressing ataxia of the lower extremities, later involvement of the arms, defective vision, paresis of ocular muscles, imperfect articulation and exaggeration of deep reflexes, including ankle-clonus. Unfortunately, autopsies are wanting.

Somewhat different are the cases (a sister and two brothers) reported by Rossolimo[32]. There was no evidence whatever of previous or collateral members of the family having had any similar affection. The sister, 29 years old, had always been rather clumsy in her movements, and only middling bright mentally, but there was no progress of symptoms until after a severe accident at the age of twenty. She was found to have advanced ataxia, involving the hands which were also tremulous, paresis of one superior oblique and exaggeration of the knee-jerks. One brother, 24 years old, developed in a perfectly normal way and remained well until the age of eighteen, when, after a severe febrile illness, he began to develop the symptoms of hereditary ataxia. Prominent were the characteristic gait, ataxia of the hands, paresis of one internal rectus, over-action of facial muscles, exaggerated knee-jerks and slight ankle-clonus. In the next younger brother nothing abnormal was noticed until the age of thirteen, when he began to have an uncertain gait. Examination showed incoördinate over-action of facial muscles, imperfect articulation, ataxia, and paresis of one internal rectus. No mention is made of reflexes.

About 1894 Dr. I. H. Neff[33] published a series of cases in one respect more remarkable than any on record; viz., the age at onset. He had an opportunity of examining only two cases (sisters), but if we may suppose the other cases in the family, traced by correspondence and personal interview, to have been the same disorder, there were thirteen cases in four generations and the disease never began under the age of fifty-five. One patient in whom it began at sixty was still living at eighty-six, unable to walk but mentally clear, and in two instances it began at seventy-two. In his first case the trouble began at fifty-five years, the first symptom being incoördination in walking. Then followed pains, not severe, in the back and legs. At fifty-eight, the arms and hands showed ataxia, and six months later speech became hesitating and stammering. A year after this she had become quite helpless, but presented no mental symptoms. At seventy-two years she began to exhibit irritability with occasional confusion and persecutory delusions alternating with depression. At this time incoördination of the lower extremities was extreme. The arms showed ataxia and volitional tremor. Speech was slow, ataxic and explosive, accompanied by tremor of facial muscles. The pupils were equal in size and reacted normally, vision unaffected. The inner surfaces of the legs were slightly anesthetic and sensation seemed delayed, probably in consequence of the mental state, as there was some dementia. The knee-jerks were active and slight ankle-clonus was elicited on the right side. Faradic excitability is said to have been increased. Six months later occasional twitching of the eyes could be observed when the patient fixed, and the pupils reacted sluggishly to light. Three months after this their reaction was normal.

His second case was a counterpart of the first except that the disease began ten years later, and that possibly optic atrophy developed in the terminal stage. One of these patients was an inmate of the asylum at Kalamazoo, Michigan, and the superintendent, Dr. William M. Edwards, has kindly furnished me the following additional information:

She lived more than five years after Neff's last note and about a year before death her condition, briefly, was as follows: While possessing a fair degree of strength, incoördination was so marked that she could walk only a few steps without assistance, and the movements of face, tongue and upper extremities were also extremely ataxic. The knee-jerks were slightly decreased except on reënforcement and the pupillary reflexes were normal. The patient was quite deaf and "failing some in vision"—cause not stated. Aside from slight depression at times, her mental state was normal. At the autopsy, "examination of the brain and spinal cord revealed no gross changes excepting adherence of the dura in the frontal region and shallowness of the fissures." A microscopic examination has been made at the Pathological Department of the Michigan State Asylums, whence a full report will issue. The note sent to Dr. Edwards is simply to the effect that there were present atrophy of the cerebellum, degeneration of the cerebellar tracts of the cord, and marked arterio-sclerosis of cerebral vessels. So far as known, then, this case scarcely sustains the contention of Marie.

Illustrative of how cases may adhere to the schema of Marie in some particulars and entirely depart from it in others, the case of Legrain[34] (de Bougie) may be cited. The mother, four maternal aunts and the maternal grandfather had died between forty and fifty, of an affection diagnosed "ataxia," and an elder brother had died at thirty-two of a similar disease. In the patient, uncertainty of gait began at the age of thirty-one, and at thirty-eight, when examined by the author, incoördination was marked in the upper as well as the lower extremities. The deep reflexes were exaggerated, sensation and mentality intact. Eye symptoms were entirely wanting and in addition to the disorder of motion, there were observed, when the patient was at rest, constant slight choreiform movements of different parts of the body—muscular inquietude. It is also to be noted that beginning two years after the onset of his malady, the patient suffered for two years with excruciating pains in thighs and calves, associated with muscular cramps of extreme severity.

In the same category of aberrant cases, cases that really adhere to no type and yet might be thought to fall within the limits of hereditary cerebellar ataxia, belongs the case of Collins[35]. The only indication of hereditary family disease was that the preceding child, who had died at the early age of two years, had not developed normally and *probably* had some incoördination. In the patient, a boy eleven years old, imperfect gait had been noticed as early as the third or fourth year. Having started to school at five, he was still in the same grade. In his tenth year he had some kind of acute attack, in which the left side became useless and thereafter there were exacerbations of incoördination on one side or the other. At eleven, he had an uncertain gait and fell easily. There were also present ataxia of the upper extremities, involvement of speech, over-action of the facial muscles and right *pied bot.* The pupils were slow to light and accommodation.

Who can at present say where the three cases of Nolan[36] belong? He reports them as cases of Friedreich's disease, (hereditary ataxia), associated with genitous idiocy, and while asserting that they were "without doubt" examples of Friedreich's disease, he notes points of resemblance to Marie's disease, the peripheral hereditary ataxia of Dejerine and Sottas[37], and family cerebral diplegia. The patients were the third, fifth and eighth children of the same family, the ages were twenty-two, fifteen and ten years respectively, in each case symptoms were noticed soon after birth, although the disease was gradually progressive; mental impairment and incoördination were present in all. Two had no knee-jerks, which would indicate Friedreich's disease, but in the second patient they were exaggerated. Furthermore, the pupils reacted normally in all three. All showed speech defect and nystagmus, two slight strabismus, but all normal vision. The first and second patients had some analgesia of the extremities, and the second and third wasting of the small hand muscles.

In a recent exhaustive paper on family diseases, Bäumlin[38] calls attention to many variations of Friedreich's ataxia and sundry inconsistencies of Marie's disease, and also reports a group of four sisters who presented clinically a certain similarity to the latter, but who suffered, he believes, with Westphal's[39] pseudo-sclerosis. In any event, the careful autopsy made in one case revealed nothing but very slight chronic meningitis.

The difficulty of asserting the type which Marie so loosely defines is manifest in the presence of cases like that described by Spiller[40]. It appears to have been congenital in origin, or at least to have begun in extreme infancy, to have presented no very distinct ataxia, but marked mental impairment, and to have been scarcely at all progressive from infancy to the age of nineteen when the patient succumbed to tuberculosis. He was microcephalic and at the autopsy not only was the cerebellum found to be small, but the corpus callosum was almost wanting and the left cerebral hemisphere was markedly atrophic. In the same article three other cases of cerebellar disease are reported, very similar to this one, but not included in the same category by the author.

Cases such as that reported by Knopfelmacher[41] are far from rare and yet he endeavors to approximate it to hereditary cerebellar ataxia. A boy of six years exhibited speech defect and incoördination which had been noticed from earliest childhood and had remained non-progressive. The case resembled hereditary cerebellar ataxia only in the presence of these symptoms and exaggerated knee-jerks, but it is only fair to hold Marie himself in part responsible for such irresponsible classification, because he has defined a certain group with such comprehensive and elastic definition as covers a multitude of sins.

Quite similar to the foregoing case is the one reported by Redlich[42], but this author at once says that the resemblance to Marie's type is superficial only. The patient, *aet.* fifty-two had some acute illness at the age of two years and was thereafter "paralyzed and blind." He presented all the more important signs of hereditary cerebellar ataxia, but Redlich, very properly, I think, considered the cause to be an acute inflammation at the time of onset, followed by atrophy and sclerosis.

After this paper was quite finished except some verbal corrections, came the *Revue de Médicine* for September, 1901, containing the admirable article of Thomas and Roux. Their paper seems to render what I have written quite superfluous, because it is so conclusive as to render discussion profitless. These authors made a complete and exhaustive post-mortem examination of one of the patients reported clinically by Klippel and Durante—one of Marie's basal cases. They found a small central nervous system, especially small cord and nerve roots. With the microscope were revealed: some atrophy of the gray matter of the cord, especially the columns of Clarke and root of the anterior horns; atrophy of the nucleus of the lateral tract in the medulla; partial degeneration of the posterior columns, principally of the columns of Goll in the cervical region; degeneration of Gowers' tract in dorsal and cervical regions and degeneration in the central part of the restiform body. The small size of the nerve roots (anterior and posterior) was most pronounced in the lumbo-sacral region, and was due not to degeneration, but to the exceeding fineness of the nerve fibers. The cerebellum was normal.

In this paper I first learned that two pupils of Marie have reported the post-mortem findings in another of Klippel and Durante's patients. Apparently there is some confusion in Marie's camp for, strange as it may seem, the first, Vincelet,[43] regards the case as one of Friedreich's disease while the second, Svitalski[44] calls it hereditary cerebellar ataxia. The former found a small cord, sclerosis of the posterior columns well marked in the lumbar region, less in the dorsal region. In short, changes much like those of Friedreich's disease with something added. The latter found in the medulla degeneration of the direct cerebellar tract and the nucleus of the column of Goll. The remainder of the medulla was normal, but small. In the pons there was diminution of the fibers of the middle cerebellar peduncle and thickening of sub-ependymal tissue of the fourth ventricle and aqueduct. The number of convolutions of the cerebellum was finished; the fissures were deep and wide. Minute changes were found between the molecular and granular layers of the cerebellar cortex, and the central white matter was small and stained poorly. There was proliferation of connective tissue in the right optic nerve. In nerve roots and peripheral nerves the number of large fibers was diminished, and the small fibers were increased. It is quite evident that the cerebellar changes were less pronounced and of less significance than those in the cord.

And finally, Dr. Lewellys F. Barker informed me a few days ago that the cords from Brown's two cases show well-defined degeneration, while the cerebellar findings, so far as the examination has been made, are extensively negative.

Doubting the existence of a disease meriting the title hereditary cerebellar ataxia, I have still for convenience called my case by this name. Should there really be such a malady, I am naturally in doubt as to whether I am reporting an example of it.

A. V. B. was first seen December 3, 1899, through the kindness of Dr. E. M. Smith[45]. He was almost nineteen years old at that time. As far as known the ancestry is excellent. Both parents are living and in good health. They are not blood relatives, there is no discrepancy in age (now 53 and 58), and no evidence of either having had syphilis. The mother, married at eighteen, has been pregnant nine times. All children have been boys. The first child is said to have died of a fall and brain fever. At seven months he fell from a high-chair, was immediately limp and then stiff, but soon regained consciousness and apparently suffered from no grave consequences. The mother states that he was not so bright and lively after the fall, and about three weeks later developed cerebral symptoms, and died at eight months. The second child had congenital heart disease, was a "blue baby" and died of exhaustion at three months. The third child was normal, grew to manhood and was perfectly well when I first saw my patient. Some months later he contracted scarlet fever followed by nephritis, of which he died. The fourth pregnancy was terminated by a miscarriage in the third month, cause unknown. Eight years after the birth of the third child the fourth was born, the miscarriage having intervened. This boy was Frank of whom I shall speak presently. Fifteen months after this birth the sixth pregnancy resulted in a still-birth at eight months, presumably from over-lifting. About four years after Frank, my patient, was born. The next child followed in three and a half years, is living, and a picture of health. The seventh child, result of the ninth pregnancy, died at eighteen months, of bronchitis and cholera morbus after an illness of four weeks.

The boy Frank was apparently entirely normal as a young child, and at the usual age entered school where he seemed to be quite up to the average in intelligence. When ten or eleven years old a gradual change in character began. He became very timid and must have shown some peculiarities, as the other children teased and pursued him. Nevertheless, he continued at school until about fifteen years old, but made very little progress. When about thirteen he developed a *penchant* for grubbing in garbage boxes, played truant, and by degrees became a good-natured, weak-minded runabout. At the age of four or five he had been struck by a street car, and when fifteen or sixteen fell down a flight of stairs, but neither of these accidents was severe or immediately followed by bad effects. Unsteadiness in walking became apparent when he was sixteen and a half years old, and was progressive. Incoördination soon invaded the upper extremities, and it is distinctly stated that the left side (leg and arm) was much worse than the right. This disability of the left arm and leg seems to have been in part paretic and not due entirely to ataxia. Within a year of the beginning of motor trouble the left side was nearly useless, and after a time developed contractures. Speech began to be affected six months after the ataxia began, that is, three and a half years before death, and gradually grew worse until it was quite lost shortly before death, the patient uttering only unintelligible sounds. Incoördination was steadily progressive; he deteriorated mentally to the point of idiocy; finally became extremely emaciated and completely paralytic, and died at the age of twenty. There is no history of eye symptoms. Incontinence was present during the last year of life, and bed-sores appeared before the end. It may be worthy of mention that once during his illness when he scalded the right leg by spilling soup upon it, apparently no pain was felt.

My patient was born at full term four years after this older brother. The labor was normal. He learned to walk and talk at the proper age, did not wet the bed later than normal, cut his teeth sufficiently early, had neither eruptions, convulsions nor any severe illness. As a child he seemed to be quite as other children, attended the public schools until fourteen or fifteen years old, where his standing and progress were satisfactory, and then procured a position as messenger and general utility boy in a store, where his services were also satisfactory until about a year and a half before my first examination. That is, the trouble began three and a half years ago. The first symptom to appear was unsteadiness of gait, to which were soon added general nervousness and irritability. He then became forgetful, so that it was necessary to write down the details of errands and the like. These signs of mental impairment dated back nearly a year. Since that time progress for the worse had been rather rapid, and four to six months before, it was noticed that speech was affected. When examined, his mentality seemed to be about that of a child of six or eight. He could read, but with numerous mistakes; he was unable to repeat even the "twos" of the multiplication table, and memory was very defective. Irritable, rebellious, transiently morose, changeable, tickled by trifles, he presented the clinical picture of an ordinary imbecile. Speech was slow, mouthing, a little indistinct and rather hesitating, not scanning, not explosive, and, on the whole, scarcely more imperfect than the mental condition. In fact, it much resembled that of some patients with infantile cerebral paralysis and imbecility. It lacked the tremulousness, slurring, varying voice and omissions of general paresis. General nutrition was apparently but little interfered with, although the boy was rather thin. Thoracic and abdominal viscera were normal, as were also the sphincters. The gait was distinctly ataxic and somewhat, far from purely, of the cerebellar type. In standing, incoördination was easily apparent, although the boy could stand with feet together. In neither station nor progression was the ataxia increased by closing the eyes, and in walking he did not regard the floor as does a tabetic. The upper extremities were also incoördinate, although to a less extent than the lower; in picking up small objects the hand "hovered" for an instant before prehension, and excess of movement was often apparent. There was no tremor of any part, in action or at rest. During speech, over-action of the facial muscles was very evident, predominating at different times in different parts of the face. Often this gave an appearance of one-sided paresis really not present. Indeed, there was no paralysis to be found anywhere; neither was there atrophy or deformity. The arch of either foot was unusually high, but could not be affirmed to be pathological, the toes were normal in position and motion, the spinal column normal. Owing to the mental condition the examination of sensation was not very satisfactory, but apparently it was normal. Certainly no marked defect was present. Pain had not been a symptom at any time. The pupils were large, equal, slightly irregular, did not respond to light and very slightly, if at all, to accommodation. Movements of the eyes, vision, the fundi oculi and hearing were normal. The deep reflexes were all exaggerated except the jaw-jerk which could not be elicited. Ankle-clonus was absent, although the ankle-jerk was so excessive as to lead me to expect its presence. At this time and for some months thereafter he amused himself a great deal of the time by copying verses. When first seen this was done with fair accuracy and good chirography. A specimen two months later showed mistakes of omission and commission and some irregularities in penmanship. The appetite was capricious, but on the whole good, bowel and bladder functions said to be undisturbed, deglutition free, sleep normal.

A diagnosis of hereditary cerebellar ataxia was made, but to be on the safe side an active course of anti-syphilitic treatment was advised. Accordingly, Dr. Smith put him on inunctions of mercury and rapidly increasing doses of potassium iodide, but the patient soon grew worse, in fact became bedfast from weakness, and the treatment was stopped. He quickly regained almost his former condition and then gradually lost ground.

Examination November 22, 1900, nearly a year after the former one, revealed simply moderate physical and mental change for the worse. He was thin and rather pale, walked with the feet rather far apart and with short, irregular, rather jerky, stiffish steps, steadying himself by pieces of furniture as opportunity offered, although he could walk without support of any kind. The gait was not at all typical of cerebellar disease, having very little of the wide swaying and body reeling in its make-up. Ataxia of the upper extremities was slightly worse than before. Tremor was still absent. The high arch of the feet had not changed. On stroking the sole of either foot the great toe was at once hyperextended, the movement differing from the typical Babinski sign in that it was very prompt, and thick. This reflex was more pronounced on the left side. Ankle-clonus was present on the right side and an indication of it on the left. Speech was slow, indistinct, with an occasional stutter and much "mouthing"—not unlike that of a very drunken man. Funeral was pronounced fun'l; November, Nowember; Sedgwick, Sed'k; electric lights, 'lec' 'ligh'. Overaction of the facial muscles was marked. The lips were pouted, or retracted, corners of the mouth drawn back, brows strongly elevated, then drawn down and together, etc. Frequently the first two or three words of a sentence were repeated, before the whole was delivered. Mentally there was little change. To questions in figures he responded as follows: "6 times 6 equals 66; 5 times 5 equals 25; 3 times 25 equals 75; 6 times 7 equals 49; 2 times 8 equals 16; 4 times 25 equals a dollar; 5 times 25 equals a dollar and a quarter." Despite the dementia and facial overaction, at times almost amounting to contortion, the face was very far indeed from being expressionless. When he was pleased and laughed, the face lighted up, and when displeased or resentful the play of expression was equally striking. When at rest the features certainly lacked expression.

During the past year degeneration has been more rapid. The boy now (November 1901) is much emaciated, eyes sunken and not entirely closed in sleep, face pale and smooth as if the skin were stretched over it. The tongue is coated and there are sordes on teeth and lips. This condition may be due in part to obstinate constipation. When the bowels move there is incontinence and consequently the mother, who has entire care of him, causes an evacuation only about once a week. Incontinence of urine is also present. Ataxia has reached a degree making it impossible for him to walk without assistance and almost impossible for him to feed himself. Speech has been steadily growing worse until now it may be said to have disappeared. He apparently attempts to talk but only inarticulate sounds result; yes and no are at times barely distinguishable. Phonation is intact. Occasionally he has shouting or screaming spells when he can be heard all over the neighborhood. Without ascertainable cause he becomes destructive, tearing bedding or his clothes to shreds. He is never violent but may refuse food or resist being dressed, undressed or cleaned, and on such occasions may attempt to scratch or even bite. Besides the screaming spells, there are times when he repeats the same expression, as "la-la-la," over and over. The brother did the same thing, and before losing speech would repeat a word in the same way, sometimes for minutes together without intermission. As the forgoing indicated, A. is now demented. He seems to understand very little, but I am sure recognizes me, and his face lights up much as it did at first, with excessive rising of the eyebrows, opening of eyes and wrinkling of forehead. Pupils and deep reflexes are unchanged, except that at my last visit I could get no ankle-clonus. Muscular strength is fair and tremor absent as heretofore. Vision seems to be good. A few weeks ago he could recognize his name written with a pencil in an ordinary hand, and made a not altogether unsuccessful attempt to copy it. At that time he could not articulate a word. His mentality, therefore, is quite above his power of speech.

In this case the progressive mental failure, rigid pupils, ataxic gait with exaggerated reflexes and indistinct speech, together with the history of miscarriages and deaths in infancy, at once suggest precocious general paresis due to inherited syphilis. On this supposition the elder brother may have had the same disease, or, bearing in mind the hemiplegia, syphilis hereditaria tarda. Remembering that precocious paresis is apt to be atypical, I have had this possibility constantly in mind. Even now I have no inclination to be dogmatic on the subject, but the case has never looked to me like general paresis, and I think that diagnosis could not be maintained. Adequate evidence of syphilis in the parents is wanting. What Freud[46] noticed in the family of his diplegics and called *eine Neigung zur Leichtsterblichkeit* (vital vulnerability), in my opinion explains the early deaths and miscarriages in the family as well as does the theory of specific disease. Incoördination distinctly antedated mental deterioration, and has throughout dominated the clinical picture. No trace of a delusion has ever been detected; tremor of lips, tongue and hands has been consistently absent. In addition, absence of the Argyll-Robertson pupil, of analgesia of the legs, of good-natured self-satisfaction and mental depression alike, would tend to exclude paretic dementia. Extreme over-action of the facial muscles is no part of the symptomatology of this disease, and by this time there should be more motor feebleness than is the case.

Granted that there is very considerable resemblance of my case to general paresis, it is but reasonable to suppose that the histological changes are not widely different from those of the latter disease. But how is it possible to reconcile such a state of affairs with cerebellar wasting as the anatomical basis of hereditary cerebellar ataxia? It is not possible. It were as reasonable to call my case merely one of Friedreich's disease with mental symptoms. In the light of all the symptoms exhibited by Marie's basal cases and by those since reported, but especially in the light of discovered changes in the central nervous system, it is almost preposterous to ask one to believe that the whole symptom-complex is caused by degenerative changes in the cerebellum. In this connection, too, it is well to remember that the combined sclerosis of Friedreich's disease is far from explaining all the symptoms of that disease. To account for the nystagmus, disordered speech and changed facial expression we are almost forced to assume changes at least as high as the pons and cerebellum, and when mental defect appears, as is sometimes the case, still higher involvement must be present. If by hereditary cerebellar ataxia we may understand an hereditary, or at least a family, disease of those systems of neurones, afferent and efferent, having to do with the cerebellar function, the name could be provisionally tolerated. Otherwise, it should be at once suppressed or restricted to a class of cases not yet discovered. For the present it would seem wise to follow the example of Sanger Brown and confine ourselves to the simple term "hereditary ataxia." Five or six years ago[47] in reviewing Londe's monograph, I said: "In brief, hereditary cerebellar ataxia is to be distinguished clinically from Friedreich's disease by the absence of certain symptoms, all of which it may in time take on, and by the frequent presence of eye symptoms, generally absent in the latter; but the latter may in turn take on these same ocular symptoms. Pathologically we have in hereditary cerebellar ataxia an atrophy of the cerebellum, with at times certain changes in the spinal cord; in Friedreich's disease, these same cord changes and at times (not always, as Senator would have it) an added cerebellar atrophy. It seems reasonable, then, to conclude that in these two affections we have but one disease, affecting a sensori-motor system concerned with coördination and equilibration, and that as one or the other part of the system is first or exclusively affected, so the clinical picture will vary." Later I learned that Edinger[48] had expressed practically the same opinion. This opinion must now be modified to the extent of excluding cerebellar atrophy without involvement of the cord, as there have been no autopsies which would support such a supposition. It should also be amplified to the extent of distinctly affirming at least occasional cerebral involvement.

The relation of mental failure to the somatic signs is yet to be worked out *de novo*. Knowing as little as we do of the connections of the neurones of motion, coördination and equilibration with those of the higher mental faculties, to discuss why some patients with hereditary ataxia should become dements and others remain intellectually intact to the end, were mere speculation. Whether the cerebral degeneration, necessarily underlying the mental failure, occurs as part of a huge system disease or simply as a coincidence in an organism prone to deterioration because of inborn frailty, or because of two quite distinct inherited tendencies, or by reason of some law of associated dissolution as yet unsuspected, is not to be stated at present.[49]

[1] Marie, Semaine Médicale, p. 444.

[2] Fraser, Glasgow Medical Journal, 1880. Fasc. 1.

[3] Nonne, Archiv für Psych., 1891, xxii, p. 283.

[4] Sanger Brown, Brain, 1892, p. 250.

[5] Klippel and Durante, Revue de Médicine, Oct. 1892, p. 745; Semaine Médicale, 1892, p. 467.

[6] Homén, Archiv für Psychiatrie, 1892, Bd. 24.

[7] Freud. Neurolog. Centralb., 1893, pp. 512 and 542. Higier. Deutsche Zeits. f. Nerv. ix., p. 1. An interesting and complete paper with very full literature. Haushalter, Rev. de Méd., 1895, p. 434. Bouchard, Rev. Neurolog., 1894, No. 1. Brower, Medicine, January, 1897.

[8] Ormerod, Brain, 1892, p. 268.

[9] Bernhardt, Idem, p. 278.

[10] Archiv. f. Psychiatrie, 27, p. 481.

[11] Adolf Meyer, Brain, 1897, p. 276.

[12] Not made by Meyer.

[13] Brissaud, "Leçons sur les Maladies Nerveuses." Series of 1893-94, pp. 43 and 61. Brissaud and Londe. Revue Neurol., March 15, 1894.

[14] Londe, Semaine Médicale & Revue Neurol., October 1, 1894.

[15] "Hérédo-ataxie Cérébelleuse." Paris, 1895.

[16] Neurol. Centralb., 1890, p. 378.

[17] Seeligmüller, Archiv f. Psychiatrie, Vol. x., p. 222.

[18] Nonne, Archiv f. Psychiatrie, Vol. xxvii, p. 479.

[19] Menzel, Archiv f. Psychiatrie, Vol. xxii. p. 160.

[20] Senator, Berl. kl. Woch., 1893, p. 489.

[21] Schultze, Berl. klin. Woch., August, 1894.

[22] Berl. kl. Woch., 1894, Nos. 28 and 33.

[23] Fornario, Annali di Neurologia, 1891, Fasc. vi. Abstract in Journal of Nervous and Mental Disease, 1895, p. 381.

[24] Oulmont and Ramond, Mercredi Méd., 1895, p. 97.

[25] Howard Gladstone, Brain, Winter Number, (No. 88) 1899, p. 615.

[26] Starr, Jour. of Nerv. and Ment. Disease, 1898, p. 175.

[27] Raymond, "Leçons sur les maladies du système nerveux. Series 1896-1897, p. 329.

[28] Hodge, British Medical Journal, June 5, 1897, p. 1405.

[29] Paravicini, Correspondenzblatt für Schweizer Aerzte, 1901, No. 10. Neurolog. Centralb. Nov. 16, 1901.

[30] K. Miura, Japanese Publication. Abstract in Brain, 1900, p. 345.

[31] Lennmalm, Nord. Med. Ark., 1897, N. F. viii., No. 29. Neurolog. Centralb. 1893, p. 560.

[32] Rossolimo, Abstract in Neurolog. Centralb., 1898, p. 566.

[33] I. H. Neff, Amer. Jour. Insanity, Vol. 51, (1894-5) p. 365.

[34] Legrain, "Sur un ças d'hérédo-ataxie cérébelleuse." Paris (Maloine.)

[35] Collins, Med. Record, December 21, 1895.

[36] Nolan, Dublin Jour. of Med. Science, Vol. 99, p. 370.

[37] Dejerine and Sottas, Mem. d. l. Soc. de Biol., Vol. v, series 9.

[38] Bäumlin, Deuts. Zeits. f. Nerv. Bd. xx, p. 265.

[39] Westphal. Archiv für Psychiatrie, Vol. xii. Strümpell, Deuts. Zeits. f. Nerv. Vol. xii, p. 115, and Vol. xiv, p. 348.

[40] Spiller, Brain, 1896, p. 588.

[41] Knoffelmacher, Wiener med. Bl., 1897, No. 22, Neurolog. Centralb. 1897, p. 1064.

[42] Redlich, Wiener med. Woch. 1896, No. 19. Neurolog. Centralb., 1895, p. 682.

[43] Vincelet, "Etude sur l'anatomie pathologique de la maladie de Friedreich."

[44] Svitalski, "Sur l'anatomie pathologique de l'hérédo-ataxie cérébelleuse." Rev. Neurol. 1901, No. 3.

[45] He was shown to the Chicago Neurological Society, January 18, 1900.

[46] Freud, *loc. cit.*

[47] Gould's Year-Book, 1896, p. 631.

[48] Real-Enclyclop. d. gesammt. Heilk. 1895, Vol. vii, p. 117.

[49] Since the above was written my patient has died. To the naked eye the brain was normal except that the cerebellum seemed rather small, not reaching to the posterior pole of the cerebrum.